

US EPA ARCHIVE DOCUMENT



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

Caswell  
11074  
#  
723K

JUN 16 1994

OFFICE OF  
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: RfD/Peer Review Report of Myclobutanil (Rally) [Alpha - butyl-alpha-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile].

CASRN. 88671-89-0  
EPA Chem. Code: 128857  
Caswell No. 723K

FROM: George Z. Ghali, Ph.D.  
Manager, RfD/Quality Assurance Peer Review  
Health Effects Division (7509C)

*Richard J. Whately*  
6/16/94  
for

TO: Steven Robbins, PM 21  
Fungicide-Herbicide Branch  
Registration Division (7505C)

Lois Rossi, Chief  
Re-registration Branch  
Special Review and Re-registration Division (7508W)

The Health Effects Division RfD/Peer Review Committee met on April 28, 1994 to discuss and evaluate the existing and recently submitted toxicology data in support of Myclobutanil re-registration and to re-assess the Reference Dose (RfD) for this chemical.

Material available for review included data evaluation records for a chronic toxicity/carcinogenicity study in rats (83-5 or 83-1a and -2a), a carcinogenicity study in mice (83-2b), a chronic toxicity study in dogs (83-1b), developmental toxicity studies in rats and rabbits (83-3a and -3b) a multi-generation reproductive toxicity study in rats (83-4), and subchronic toxicity studies in rats, mice and dogs (82-1a and -1b).

The Committee considered the chronic toxicity study in rats (83-1a, MRID No. 42809101; 00149582, 00165247) and dogs (83-1b, MRID No. 00149583, 00165248) to be acceptable and the data evaluation records (HED Doc. No. 00000, 006580; 006580) to be adequate.

The carcinogenicity issue had been discussed by the Health

Effects Division-Carcinogenicity Peer Review Committee (HED-CPRC) in their meeting of February 9, 1988. At that time, the CPRC concluded that the dose levels tested in male and female rats and female mice were not adequate for carcinogenicity testing. The CPRC proposed to the registrant appropriate dose levels to be used in the repeat studies.

In the meeting of April 28, 1994, data evaluation records for the original carcinogenicity studies in rats (83-2a, MRID No. 00149582, 00165247) and mouse (83-2b, MRID No. 00164990, 40244301) along with the data evaluation records of the new carcinogenicity studies in rats (MRID No. 00149582, 00165247) and mice (MRID No. 00164990, 40244301) were made available to the RfD Committee for review. The Committee considered the carcinogenicity studies in rats and mice to be acceptable and the data evaluation records (HED Doc. No. 006580) to be adequate. The treatment did not alter the spontaneous tumor profile in either species. The chemical was classified as a "Group E".

The Committee considered the reproductive toxicity study in rats (83-4, MRID No. 00143766, 00149581), the developmental toxicity study in rats (83-3a, MRID No. 00141672) and rabbits (MRID No. 00164971) to be acceptable and the data evaluation record (HED Doc. No. 006580; 004937; 006580) to be adequate. There was no evidence, based on the available data, that myclobutanil was associated with significant reproductive or developmental toxicity under the testing conditions.

The RfD for this chemical was first determined by the Health Effects Division - RfD Committee on April 10, 1987 and was then reassessed on January 27, 1988 and was verified by the Agency RfD Work Group on February 25, 1988. At that time, the RfD was based on a chronic feeding study in rats with a NOEL of 2.49 mg/kg/day. Testicular atrophy was observed at 9.84 mg/kg/day and higher dose levels. An uncertainty factor (UF) of 100 to account for the inter-species extrapolation and intra-species variability. On this basis, the RfD was calculated to be 0.025 mg/kg/day. In the meeting of April 28, 1994, the Committee recommended that the RfD remains unchanged. It should be noted that this chemical has not been reviewed by the World Health Organization (WHO) up to this date.

A. Individuals in Attendance

1. Peer Review Committee Members and Associates Present  
(Signature indicates concurrence with the peer review unless otherwise stated).

William Burnam

Reto Engler

Karl Baetcke

Marcia Van Gemert

Henry Spencer

William Sette

Esther Rinde

Roger Gardner

James Rowe

George Ghali

Rick Whiting

2. Scientific Reviewer (Committee or non-committee members responsible for data presentation; signatures indicate technical accuracy of panel report).

Pam Hurley

Roger Gardner

3. Others:

E. Budd and D. Liem of HED as observers.

CC: Penny Fenner-Crisp  
Richard Schmitt  
Kerry Dearfield  
Karl Baetcke  
Roger Gardner  
Pam Hurley  
James Kariya  
Flora Chow  
RfD File  
Caswell File

*W. Burnam*  
*Reto Engler*  
*Karl Baetcke*  
*Marcia van Gemert*  
*Henry Spencer*  
*William Sette*  
*Esther Rinde*  
*Roger Gardner*  
*James N. Rowe*  
*George Ghali*  
*Rick J. Whiting*

*Pamela M. Hurley*  
*Roger Gardner*

B. Material Reviewed

Material available for review included data evaluation records for a chronic toxicity/carcinogenicity study in rats (83-5 or 83-1a and -2a), a carcinogenicity study in mice (83-2b), a chronic toxicity study in dogs (83-1b), developmental toxicity studies in rats and rabbits (83-3a and -3b) a multi-generation reproductive toxicity study in rats (83-4), and subchronic toxicity studies in rats, mice and dogs (82-1a and -1b).

1. Shellenberger, T. E. et al. (1986). Chronic toxicity and oncogenicity study with RH 3866 in rats. MRID No. 00149582, 00165247, HED Doc. No. 006580. Classification: Core Guideline for chronic toxicity and Core-supplementary for carcinogenicity. This study, in conjunction with another study cited below, satisfies data requirement 83-1a and 83-2a of Subpart F of the pesticide Assessment Guideline for chronic toxicity/carcinogenicity testing in rats.
2. Wolfe, G. W. (1993). RH-3866 technical (Myclobutanil): 104-week dietary oncogenicity study in rats. MRID No. 42809101, HED Doc. No. 000000. Classification: Guideline when viewed together with another study cited under MRID No. 00149582, 00165247 above. This study, in conjunction with the previous study, satisfies data requirement 83-2a of Subpart F of the Pesticide Assessment Guideline for carcinogenicity testing in rats.
3. Goldman, P. R. and Harris, J. C. (1986). RH-3866: dietary chronic and oncogenicity study in mice. MRID No. 00164990, 40244301, HED Doc. No. 000000. Classification: Core-Guideline for chronic toxicity and Core-supplementary for carcinogenicity. This study, in conjunction with another study cited below under MRID No. 42809102, satisfies data requirement 83-2b of Subpart F of the Pesticide Assessment Guideline for carcinogenicity testing in mice.
4. Anderson, D. M. et al. (1993). RH-3866: dietary oncogenicity study in female mice. MRID No. 42809102, HED Doc. No. 000000. Classification: Core-minimum when viewed together with another study cited under MRID No. 40244301 cited above. This study, in conjunction with the previous study, satisfies data requirement 83-2b of Subpart F of the Pesticide Assessment Guideline for carcinogenicity testing in mice.
5. Goldman, P. R. and Harris, J. C. (1986). RH-3866: one-year dietary study in beagle dogs. MRID No. 00149583, 00165248, HED Doc. No. 006580. Classification: Core-minimum data. This study satisfies data requirement 83-1b of Subpart F of the Pesticide Assessment Guideline for chronic toxicity testing in dogs.
6. Costlow, R. D. and Harris, J. C. (1985). RH-53,866: two-generation reproduction study in rats. MRID No. 00143766, 00149581, HED Doc. No. 004936. Classification: Core-Guideline data. This

study satisfies data requirement 83-4 of Subpart F of the Pesticide Assessment Guideline for reproductive toxicity testing in rats.

7. Costlow, R. D. and Kane, W. W. (1984). Teratology study with RH-53,866 in rats. MRID No. 00141672, HED Doc. No. 004937. Classification: Core-minimum data. This study satisfies data requirement 83-3a of Subpart F of the Pesticide Assessment Guideline for developmental toxicity testing in rats.

8. Costlow, R. D. and Kane, W. W. (1984). Teratology study with RH-53,866 in rabbits. MRID No. 00164971, HED Doc. No. 006580. Classification: Core-minimum data. This study satisfies data requirement 83-3b of Subpart F of the Pesticide Assessment Guideline for developmental toxicity testing in rabbits.